

# Module 6: Depression, Dementia & Delirium

# **Geriatrics, Palliative Care and Interprofessional Teamwork Curriculum**

## **Module # 6: Depression, Dementia & Delirium**

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## **Module # 6: Depression, Dementia & Delirium**

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## **Geriatrics, Palliative Care and Interprofessional Teamwork Curriculum**

### **Module # 6: Depression, Dementia & Delirium**

#### **I. Overview**

Depression, dementia, and delirium are the three most prevalent mental disorders in the elderly. While depression and dementia are prevalent in the community, hospitals, and nursing homes, delirium is seen most often in acute care hospitals. Dementia is defined by a chronic loss of intellectual or cognitive function of sufficient severity to interfere with social or occupational function. Delirium is an acute disturbance of consciousness marked by an attention deficit and a change in cognitive function. Depression is an affective disorder evidenced by a dysphoric mood, but the most pervasive symptom is a loss of ability to enjoy usual activities. It is important to recognize that these syndromes are not mutually exclusive, as dementia frequently co-exists with delirium and depression. Furthermore, physical diagnoses, such as chronic obstructive lung disease, congestive heart failure, stroke, and endocrine disorders, are frequently associated with depressive symptoms. Given this, a comprehensive evaluation is mandatory.

#### **II. Learning Objectives**

1. Define the prevalence and symptoms of depression in the older population.
2. List depression assessment tools for use in the elderly.
3. Describe methods for managing depression in late life.
4. Describe the prevalence and symptoms of delirium in the older population.
5. Provide an overview of the assessment and treatment of delirium in older adults.
6. Define the prevalence and symptoms of dementia in the elderly.
7. Describe methods for assessing and treating dementia in older people.

#### **III. Depression**

##### **A. Prevalence**

1. In The Older Population

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- A. Depression is significantly under-diagnosed and undertreated in older adults. <sup>1</sup> Older adults and health care professionals may attribute symptoms of depression to old age or other physical conditions.
  - B. The prevalence of major depression in the general older population is 1.4% in women and 0.4% in men, with an overall prevalence of 1%. However, 17- 37% of the older *medical* population suffers from depression, with 30% of these patients suffering from major depression. <sup>2</sup>
  - C. Major depressive disorders occur less often in older adults compared to younger adults; however, older adults suffer from psychotic (delusional) depression more frequently. <sup>3</sup>
  - D. The highest rate of completed suicide of any age, gender, or ethnic group is among older white men. The risk of suicide is 50% higher in older adults than the rate for younger people.
2. In the Seriously Ill <sup>4</sup>
    - A. 25-77% of seriously ill patients experience intense feelings of sadness and anxiety accompanied by depressive symptoms, which persist for longer than a few weeks.

## B. Symptoms

### 1. Clinical Manifestations Of Depression In Older Adults <sup>5</sup>

#### A. Mood

- Depressed, irritable, or anxious (may deny sad mood and complain of pain or somatic distress)
- Crying spells (or complaining of inability to cry or experience emotion)
- Persistent for more than 14 days

#### B. Associated Psychological Symptoms

- Reduction in gratification, loss of interest in usual activities, loss of attachments, social withdrawal
- Lack of self-confidence, low self-esteem, self reproach
- Poor concentration and memory
- Difficulty making decisions
- Negative expectations, hopelessness, helplessness, increased dependency
- Recurrent thoughts of death
- Suicidal thoughts

#### C. Somatic Manifestations

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- Anorexia and weight loss
- Insomnia – early morning awakening
- Psychomotor retardation
- Agitation – common symptoms in an older person

**D. Psychotic Symptoms**

- Delusions of worthlessness and sinfulness
- Delusions of ill health
- Delusions of poverty. Evaluate delusions as 30% of elderly women already are at the poverty level.
- Depressive hallucination in the auditory, visual, and olfactory spheres (rarely)

**2. Clinical Manifestations in the Seriously Ill <sup>6</sup>**

- A. While in the general population somatic symptoms are important when making a diagnosis of depression, these symptoms are invariably present in patients with advanced illness. Therefore, psychological and cognitive symptoms are the most important signs.
- B. The most reliable symptoms of major depression in the seriously ill include persistent dysphoria, anhedonia (loss of pleasure), feelings of helplessness, hopelessness, worthlessness, and loss of self-esteem.
- C. Other symptoms include excessive guilt, pervasive despair, bothersome ruminations about death, and thoughts of suicide.

**C. Assessment Tools**

1. Geriatric Depression Scale (GDS)
2. Cornell Depression Scale (CDS)

**D. Management**

**1. Pharmacologic**

**A. In Older Adults**

- Principal regarding dosages in older adults – Start Low Go Slow
- Carefully monitor for side effects (e.g. falls, anorexia)

**B. Choosing an Antidepressant: (see Table below and list of antidepressants to avoid) <sup>7</sup>**

- i. **First-line Therapy:** Consider an SSRI for most older adults, especially those with heart conduction defects or ischemic heart disease; prostatic hyperplasia; uncontrolled glaucoma.

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- ii. Second-line Therapy: Consider venlafaxine, mirtazapine, or bupropion.
- iii. Third-line Therapy: Consider nortriptyline or desipramine for patients with severe melancholic depression.

#### IV. Antidepressants Used With Older Adults

Class, Drug	Initial Dosage	Usual Dosage	Formulations	Comments (Metabolism, Excretion)
<b>Selective Serotonin-Reuptake Inhibitors</b>				Class adverse events (EPS, hyponatremia) (L, K [10%])
Citalopram ( <i>Celexa</i> )	10–20 mg qam	20–30 mg/d	T: 20, 40, 60; S: 5 mg/10 mL	
Escitalopram ( <i>Lexapro</i> )	10 mg/d	10 mg/d	T: 10, 20	
Fluoxetine ( <i>Prozac</i> )	5 mg qam	5–60 mg/d	T: 10; C: 10, 20, 40; S: 20 mg/5 mL; C: SR 90 (weekly dose)	Long half-lives of parent and active metabolite may allow for less frequent dosing; may cause more insomnia than other SSRIs; CYP2D6, -2C9, -3A4 inhibitor (L)
Fluvoxamine ( <i>Luvox</i> )	25 mg qhs	100–300 mg/d	T: 25, 50, 100	Not approved as an antidepressant in US; CYP1A2, -3A4 inhibitor (L)
Paroxetine ( <i>Paxil</i> )	5 mg	10–40 mg/d	T: 10, 20, 30, 40	Helpful if anxiety symptoms are prominent; increased risk of withdrawal symptoms (dizziness); CYP2D6 inhibitor (L)
( <i>Paxil CR</i> )	12.5 mg/d	—	T: ER 12.5, 25, 37.5; S: 10 mg/5 mL	Increase by 12.5 mg/d no faster than 1/wk (L)
Sertraline ( <i>Zoloft</i> )	25 mg qam	50–200 mg/d	T: 25, 50, 100; S: 20 mg/mL	(L)
<b>Additional Medications</b>				
Bupropion ( <i>Wellbutrin, Zyban</i> )	37.5–50 mg bid 100 mg (SR) qd or bid	75–150 mg bid 100–150 mg (SR) bid	T: 75, 100, SR 100, 150	Consider for SSRI, TCA nonresponders; safe in HF; may be stimulating; can lower seizure threshold (L)
Duloxetine ( <i>Cymbalta</i> )	20 mg qd	20–30 mg bid	C: 20, 30, 60	Most common side effects: nausea, dry mouth, constipation, diarrhea, urinary hesitancy (L)
Methylphenidate ( <i>Ritalin</i> )	2.5–5 mg at 7 AM and noon	5–10 mg at 7 AM and noon	T: 5, 10, 20	Short-term treatment of depression or apathy in physically ill older adults; used as an adjunct (L)
Mirtazapine ( <i>Remeron</i> )	15 mg qhs	15–45 mg/d	T: 15, 30, 45	May increase appetite; sedating; oral disintegrating tab (SolTab) available (L)
Trazodone ( <i>Desyrel</i> )	25 mg qhs	75–600 mg/d	T: 50, 100, 150, 300	Sedation may limit dose; may be used as a hypnotic; ventricular irritability; priapism in men (L)
Venlafaxine ( <i>Effexor</i> )	25–50 mg bid	75–225 mg/d	T: 25, 37.5, 50, 75, 100	Low anticholinergic activity; minimal sedation and hypotension; may increase BP and QT <sub>c</sub> ; may be useful when somatic pain present; EPS, withdrawal symptoms, hyponatremia (L)
( <i>Effexor XR</i> )	75 mg qam	75–225 mg/d	C: 37.5, 75, 150	Same as above
<b>Tricyclic Antidepressants</b>				

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Desipramine ( <i>Norpramin</i> )	10–25 mg qhs	50–150 mg/d	T: 10, 25, 50, 75, 100, 150	Therapeutic serum level >115 ng/mL (L)
Nortriptyline ( <i>Aventyl, Pamelor</i> )	10–25 mg qhs	75–150 mg/d	C: 10, 25, 50, 75; S: 10 mg/5 mL	Therapeutic window (50–150 ng/mL) (L)
<b>Monoamine Oxidase Inhibitors</b>				Hypotension; drug, food interactions (K, L)
Isocarboxazid ( <i>Marplan</i> )	10 mg bid– tid	10 mg tid	T: 10	
Phenelzine ( <i>Nardil</i> )	15 mg qd	15–60 mg/d	T: 15	
Tranylcypromine ( <i>Parnate</i> )	10 mg bid	20–40 mg/d	T: 10	

<b>V. Antidepressants To Avoid With Older Adults</b>
• <b>Amitriptyline</b> (e.g., <i>Elavil</i> ): anticholinergic, sedating, hypotensive
• <b>Amoxapine</b> ( <i>Asendin</i> ): anticholinergic, sedating, hypotensive; also associated with EPS, tardive dyskinesia, and neuroleptic malignant syndrome
• <b>Doxepin</b> (eg, <i>Sinequan</i> ): anticholinergic, sedating, hypotensive
• <b>Imipramine</b> ( <i>Tofranil</i> ): anticholinergic, sedating, hypotensive
• <b>Maprotiline</b> ( <i>Ludiomil</i> ): seizures, rashes
• <b>Protriptyline</b> ( <i>Vivactil</i> ): very anticholinergic; can be stimulating
• <b>St. John's wort</b> : decreases effects of digoxin and CYP3A4 substrates; efficacy questioned
• <b>Trimipramine</b> ( <i>Surmontil</i> ): anticholinergic, sedating, hypotensive

C. In Seriously Ill Patients <sup>8</sup>

- i. **Psychostimulants:** rapid-acting psychostimulant is the best choice when reversal of depression is an immediate short-term goal. Adverse effects are minimal and they can be used alone or in combination with other antidepressants; *not* to be used in patients with cardiac disease.
- ii. **Selective Serotonin Reuptake Inhibitors (SSRIs):** usually begin to act within 2 to 4 weeks, are highly effective (70%), once-daily dosing is possible, and cause less constipation, sedation, and dry mouth than the tricyclic antidepressants, though nausea may be worse.
- iii. **Tricyclic Antidepressants:** tricyclic antidepressants may take 3 to 6 weeks to have an effect and are not recommended



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as a first-line therapy. Anticholinergic adverse effects and cardiac conduction delays are seen frequently.

- iv. Just as with older patients – “Start Low Go Slow”
- 2. Electroconvulsive Therapy: treatment of choice for older persons with severe depression; improvement rate in older persons who do not respond to antidepressant drugs is 80% (same as in younger persons).
- 3. Psychotherapy:
  - A. **In Older Adults**: especially effective in preventing relapses of episodic depression (30% relapse rate of depression in older adults); however, the practitioner must take into consideration that older adults may have negative attitudes towards psychotherapy.<sup>9</sup> For mild to moderate depression, can be in combination with pharmacotherapy: cognitive-behavioral therapy, interpersonal therapy, and problem solving therapy.
  - B. **In the Seriously Ill**: may help put perceptions, expectations, needs, fears, and fantasies about his or her illness and death into a different perspective. Relaxation, meditation, guided imagery, or self-hypnosis can also be introduced.<sup>10</sup>

## VI. Case Analysis: Ms. G \*

Ms. G is a 75 year-old female living alone in her apartment in New York City. Her husband died suddenly two years ago of a heart attack. Their two children are alive and living out-of-state. Both of her sons maintain weekly phone contact with Ms. G and visit usually once a year. Ms. G has been doing well until about 6 weeks ago when she fell in her apartment and sustained bruises but did not require a hospital visit. Since then, she has been preoccupied with her failing eyesight and decreased ambulation. She does not go shopping as often, stating she doesn't enjoy going out anymore and feels “very sad and teary”. Ms. G states that her shopping needs are less, since she is not as hungry as she used to be and “besides I'm getting too old to cook for one person only”.

### Focus Questions:

1. What risk factors might account for Ms. G's symptoms of depression?
2. What are Ms. G's depressive symptoms?
3. What might be some treatment strategies for Ms. G?

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\* Abrams WB, Beers MH, Berkow R (Eds) (1995). The Merck Manual of Geriatrics (2<sup>nd</sup> Ed). Whitehouse Station. New Jersey.

## VII. Delirium

### A. Prevalence

Delirium or acute confusional states occur in 30% of older persons during medical hospitalization and occur 10%-50% during surgical hospitalization. Most at risk are those with dementia and those of advanced age, comorbid physical problems, especially sleep deprivation, immobility, dehydration, pain, and sensory impairment.

### B. DSM-I Criteria Used to Identify Delirium <sup>11</sup>

1. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, or shift attention;
2. Change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia;
3. Disturbance that develops over a short period of time (usually hours to days) and tends to fluctuate over the course of the day;
4. Evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiologic consequences of a specific medical condition, substance intoxication, substance withdrawal, multiple causes, causes not otherwise specified, insufficient evidence to establish a specific cause, or from other reasons, such as sensory deprivation.

### C. Symptoms <sup>12</sup>

- Abrupt precise onset with identifiable date
- Acute illness, generally days to weeks, rarely more than 1 month
- Usually reversible, often completely
- Disorientation early
- Variability from moment to moment, hour to hour, throughout the day
- Prominent physiological changes
- Clouded, altered, and changing level of consciousness (alert→ lethargy)
- Strikingly short attention span
- Disturbed sleep-wake cycle with hour-to-hour variation
- Marked psychomotor changes (hyperactive or hypoactive)

**D. Assessment** <sup>13</sup>

1. Obtain a comprehensive history, including ADLs and IADLs, alcohol use, baseline cognitive function, and time course of changes in consciousness.
2. Physical examination (there may be more than one problem).
3. Review of all current medications, both over-the-counter and prescription.
4. Evaluate basic laboratory studies (complete blood count, serum electrolytes and urinalysis).
5. Consider further testing on basis of results of laboratory studies and response to initial therapy (chest radiography, cultures, drug levels, serum B12, thyroid function tests, pulse oximetry, electrocardiogram, brain imaging, lumbar puncture, electroencephalogram).

**E. Treatment** <sup>14</sup>

1. Identify and treat the underlying cause.
2. Provide supportive and restorative care: improve orientation, decrease sensory overload or deprivation, provide reassurance, provide a quiet room, and follow fixed daily schedules.
3. Treat behavioral symptoms that may result. Haloperidol sedates and treats hallucinations, paranoia, and delusions. Benzodiazepines are an alternative when sedation is the primary desired effect.
4. If psychotic symptoms are severe, frightening, or may effect safety, use antipsychotic.
6. Olanzapine, quetiapine, and risperidone are first choice because of fewer adverse events (TD extremely high in older adults taking typical antipsychotics).
7. Failure to treat delays recovery and can worsen the older person's health and function.

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## VIII. Representative Medications For Treatment Of Psychosis <sup>15</sup>

Class, Agent	Dosage*	Formulations	Comments (Metabolism)
<b>Atypical Antipsychotics</b>			
Aripiprazole ( <i>Abilify</i> )	10–15 (1) initially; max 30/d	T: 10, 15, 20, 30	Sedation; wait 2 wk between dosage changes (CYP2D6, 3A4) (L)
Clozapine ( <i>Clozaril</i> )	25–150 (1)	T: 25, 100	May be useful for parkinsonism and TD; sedation, orthostasis, anticholinergic effects, agranulocytosis, weight gain; high risk of diabetes mellitus and dyslipidemia (L)
√ Olanzapine ( <i>Zyprexa</i> )	2.5–10 (1)	T: 2.5, 5, 7.5, 10, 15, 20; disintegrating tab: 5, 10, 15, 20	Sedation, anticholinergic effects at high doses, high risk of weight gain, hyperglycemia, diabetes mellitus, risk of cerebrovascular adverse events; dose-related EPS (L)
√ Quetiapine ( <i>Seroquel</i> )	25–800 (1–2)	T: 25, 100, 200, 300	Sedation, orthostasis, no dose-related EPS; intermediate risk of diabetes mellitus and dyslipidemia; limited geriatric data (L, K)
√ Risperidone ( <i>Risperdal</i> )	0.5–1 (1–2)	T: 0.25, 0.5, 1, 2, 3, 4 scored; S: 1 mg/mL; IM long-acting: 25, 37.5, and 50 mg/2 mL	Orthostasis, dose-related EPS; caution in patients at risk of stroke, risk of cerebrovascular adverse events, intermediate risk of diabetes mellitus and dyslipidemia; IM not for acute treatment; do not exceed 6 mg (L, K)
Ziprasidone ( <i>Geodon</i> )	20–80 (1–2)	C: 20, 40, 60, 80; IM: 20 mg/mL	May increase QT <sub>c</sub> ; very limited geriatric data (L)
<b>Low Potency</b>			
Thioridazine (eg, <i>Mellaril</i> )	25–200 (1–3)	T: 10, 15, 25, 50, 100, 150, 200; S: 30 mg/mL	Anticholinergic effects, orthostasis, QT <sub>c</sub> prolongation, sedation, TD; for acute use only (L, K)
<b>Intermediate Potency</b>			
Loxapine ( <i>Loxitane</i> )	2.5–20 (1–3)	C: 5, 10, 25, 50; S: 25 mg/mL	Anticholinergic effects, orthostasis, sedation, TD; for acute use only (L, K)
<b>High Potency</b>			
Haloperidol ( <i>Haldol</i> )	0.5–2 (1–3); depot 100–200 mg IM q 4 wk	T: 0.5, 1, 2, 5, 10, 20; S: conc 2 mg/mL; Inj	EPS, TD; for acute use only (L, K)
√ = preferred for treating older adults but does not imply lower risk; mortality may be increased in patients with dementia.			
* Total mg/d (frequency/d).			

## IX. Terminal Delirium

Common in patients with advanced illnesses who are nearing death. Presents as day-night reversal and is complex; therefore, it is difficult to assess and manage. When patients who are dying experience agitation, restlessness, moaning, and/or groaning due to terminal delirium, it is usually irreversible. Management is focused on symptomatic control and relief of patient and family. Benzodiazepines or sedating neuroleptics are most effective.

## **X. Case Analysis: Mr. T \***

Mr. T is a 70 year-old male admitted to the orthopedic unit in a large urban hospital. Mr. T fractured his right ankle in a golf outing and had an open reduction with internal fixation this morning. As you take report at 3:00PM, the day shift charge nurse tells you that Mr. T is insisting on going home and keeps getting out of bed. Multiple attempts to explain that he is unable to walk safely in the cast have not convinced him and he is now yelling, disturbing other patients on the floor.

### Focus Questions:

1. Given the above information, you suspect that Mr. T's condition is caused by
  - a) post-operative infection
  - b) dementia
  - c) delirium
  - d) depression
2. Delirium:
  - a) is self-limiting and requires no intervention
  - b) usually has no identifiable cause
  - c) requires acute assessment
  - d) should be treated symptomatically
3. The causes of delirium include
  - a) infection
  - b) hypoxia
  - c) medications
  - d) all of the above
4. Some strategies to assist in caring for Mr. T would include
  - a) reality orientation offered in a calm, nonjudgmental manner
  - b) calling family to visit patient
  - c) telling him to relax and his ankle will heal
  - d) a & b only

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\* Abrams WB, Beers MH, Berkow R (Eds) (1995). The Merck Manual of Geriatrics (2<sup>nd</sup> Ed). Whitehouse Station. New Jersey.

## **XI. Dementia**

### **A. Prevalence**

Dementia, defined as a syndrome of persistent cognitive impairment in adults, occurs in 5% to 15% of older persons, with prevalence rates doubling every 5 years between the ages of 65 and 85. Twenty-five to thirty percent (25% – 30%) of persons age 85 and over have dementia.<sup>16</sup> It has been estimated that by the year 2050, there will be over 13 million persons with dementia in the US and 114 million worldwide.<sup>17</sup>

### **B. Symptoms<sup>18</sup>**

- Gradual onset that cannot be dated
- Chronic illness, characteristically progressing over years. Diagnosis based on at least six months of confusion
- Generally irreversible, often chronically progressive
- Disorientation later in the illness, often after months or years
- Much more stable day-to-day (unless delirium develops)
- Less prominent physiological changes than delirium
- Consciousness not clouded until terminal (alert but confused and disoriented)
- Attention span not characteristically reduced
- Disturbed sleep-wake cycle with day-night reversal
- Psychomotor changes characteristically late (unless depression develops)
- Depression can affect performance on mental status tests and should be considered when cognitive impairment is suspected. As discussed by Gallo and Wittink:

“The person with the appearance of cognitive impairment secondary to depression remains oriented and with coaxing can perform cognitive tests. Clues that dementia may be secondary to depression include recent onset and rapid progression, a family history of depressive disorders, a personal history of affective disorders, and onset of the disorder after the age of 60 years.”<sup>19</sup>

### **C. Assessment**

1. Use a screen for cognitive status in older adults such as the Folstein Mini-Mental Status Exam (MMSE).
2. A complete dementia evaluation should include the following.<sup>20</sup>
  - Medical and social history
  - Complete psychiatric and medical evaluation including neurological and mental state examination
  - Laboratory tests of blood and cerebrospinal fluid
  - Brain imaging
  - Evaluation of activities of daily living (ADLs)
  - Social investigations
  - Summary evaluation and planning for the future
3. Advantages of Early Diagnosis in Dementing Conditions
  - Provide a diagnostic answer and education for the patient and or family
  - Relieve the fear of an irreversible or progressive disease
  - Treat the underlying disease
  - Initiate prevention and/or rehabilitation strategies
  - Treat behavioral and cognitive symptoms
  - Plan legal and financial future while patient is still competent
  - Initiate management strategies that will postpone dependence and institutionalization

### **D. Clinical Features Distinguishing Alzheimer's Disease & Other**

#### **Types of Dementia**

- Alzheimer's Disease: Memory, language, visual-spatial disturbances, indifference, delusions, agitation
- Frontotemporal dementia: Personality change, executive dysfunction, hyperorality, relative preservation of visual-spatial skills
- Lewy body dementia: visual hallucinations, delusions, EPS, fluctuating mental status, sensitivity to antipsychotic meds
- Vascular dementia: abrupt onset, stepwise deterioration, prominent aphasia, motor signs
- Mild Cognitive Impairment: memory loss, delayed paragraph recall,

no functional impairment, normal ADL, mild executive dysfunction

## E. Progression of Alzheimer's Disease

### 1. Early, Mild Impairment (yr 1–3 from onset of symptoms) MMSE: 22–28

- Disoriented to date
- Naming difficulties (anomia)
- Recent recall problems
- Mild difficulty copying figures
- Decreased insight
- Social withdrawal
- Irritability, mood change
- Problems managing finances

### 2. Middle, Moderate Impairment (yr 2–8) MMSE: 10–21

- Disoriented to date, place
- Comprehension difficulties (aphasia)
- Impaired new learning
- Getting lost in familiar areas
- Impaired calculating skills
- Delusions, agitation, aggression
- Not cooking, shopping, banking
- Restless, anxious, depressed
- Problems with dressing, grooming

### 3. Late, Severe Impairment (yr 6–12) MMSE: 0–9

- Nearly unintelligible verbal output
- Remote memory gone
- Unable to copy or write
- No longer grooming or dressing
- Incontinent
- Motor or verbal agitation



## F. Treatment

### 1. Non-pharmacologic <sup>21</sup>

- Use personal history, life experiences, and habits as a basis for self-care and leisure activities.
- Maintain a familiar and comfortable routine that alternates activity with rest to avoid fatigue and dysfunction.
- Promote independence, autonomy, and self-directed meaningful activities by cueing the person to do as much for him/herself as possible and providing a safe, secure setting.
- Modify the physical environment to reduce misinterpretation of real-life object or events.

## XII. Pharmacological Treatment Of Cognitive Dysfunction <sup>22</sup>

- Patients with a diagnosis of mild or moderate AD should receive a cholinesterase inhibitor that will increase level of acetylcholine in brain (**see table**).
- Controlled data show modest symptomatic benefit for cognition, mood, behavioral symptoms, and daily function of cholinergic drugs compared with placebo for 1 yr, and open trials demonstrate benefit for 3 yr.
- Only 10%–25% of patients taking cholinesterase inhibitors show clinical improvement, but 80% have less rapid decline.
- Initial studies show benefits of these drugs for patients with dementia associated with Parkinson's disease, Lewy body dementia, and vascular dementia.
- Cholinesterase inhibitors have not been convincingly demonstrated to slow progression of mild cognitive impairment to dementia.
- Cholinesterase inhibitors may attenuate non-cognitive symptoms and delay nursing-home placement.
- To evaluate response:
  - Elicit caregiver observations of patient's behavior (alertness, initiative) and follow functional status (ADL and IADL).
  - Follow cognitive status (e.g., improved or stabilized) by caregiver's report or serial ratings of cognition (eg, MMSE).
- Memantine (*Namenda*) demonstrated modest efficacy compared with placebo in moderate to severe AD as monotherapy and when combined with donepezil (*Aricept*).
- Vitamin E at 1000 IU bid found to delay functional decline in AD (caution in those with cardiovascular disease because ≥400 IU may increase mortality).
- Ginkgo biloba* is not generally recommended because clinical trial results are not yet definitive, and preparations vary because such nutraceuticals are not regulated by the FDA.
- Postmenopausal hormone therapy in older women may increase risk of developing AD.

### Cognitive Enhancers

Drug	Formulations	Dosing (Metabolism)
Donepezil ( <i>Aricept</i> ) <sup>*</sup>	T: 5, 10; ODT: 5, 10; <sup>**</sup> S: 5 mg/mL	Start at 5 mg qd, increase to 10 mg qd after 1 mo (CYP2D6, 3A4) (L)

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Galantamine ( <i>Razadyne</i> [formerly <i>Reminyl</i> ])***	T: 4, 8, 12; S: 4 mg/mL	Start at 4 mg bid, increase to 8 mg bid after 4 wk; recommended dosage 8 or 12 mg bid (CYP2D6, 3A4) (L)
Extended release ( <i>Razadyne ER</i> )	C: 8, 16, 24	Start at 1 capsule daily, preferably with food; titrate as above
Rivastigmine ( <i>Exelon</i> )*	T: 1.5, 3, 4.5, 6	Start at 1.5 mg bid and gradually titrate up to 6 mg bid as tolerated; retitrate if drug is stopped (K)
Memantine ( <i>Namenda</i> [NMDA antagonist])	T: 5, 10	Start at 5 mg qd, increase by 5 mg at weekly intervals to max of 10 mg bid; reduce dose if kidney function impaired (K)
* Cholinesterase inhibitors. Continue if improvement or stabilization occurs; stopping drugs can lead to rapid decline. Adverse events increase with higher dosing. Possible adverse events include nausea, vomiting, diarrhea, dyspepsia, anorexia, weight loss, leg cramps, bradycardia, insomnia, and agitation.		
** ODT = oral disintegrating tablet.		
*** Increased mortality found in controlled studies of mild cognitive impairment.		

### **XIII. Case Analysis: Ms. D \***

Ms. D is a 98 year-old female in a skilled nursing facility with a diagnosis of Alzheimer's disease. Ms. D comes to the nursing station and appears very upset. She tells you that she is looking for her mother and asks you to help her. You start walking with Ms. D. Which of the following strategies would be helpful in assisting Ms. D?

#### True or False:

1. Telling her that her mother died a long time ago.
2. Reassuring her that everything is OK and that you will help her.
3. Attempting to distract/redirect her into a pleasurable activity (eating, singing).
4. Using reality orientation hoping to reverse her cognitive losses.
5. Asking her to help you with a small task and later you will look for her mother together.

#### More True or False Questions:

1. Cognitive losses related to Alzheimer's disease are irreversible.
2. Although pharmacologic agents may be helpful (in the presence of disturbing delusions, hallucinations), behavioral approaches to treatment are first-line in treating dementia.
3. Promoting dependence (with feeding, dressing, toileting) is advantageous for persons with dementia.
4. Compensating for sensory impairments (glasses, hearing aides) may help minimize disturbing illusions / delusions.

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\* Abrams WB, Beers MH, Berkow R (Eds) (1995). The Merck Manual of Geriatrics (2<sup>nd</sup> Ed). Whitehouse Station. New Jersey

#### **XIV. General Guidelines For Differentiating Depression, Delirium, and Dementia <sup>23</sup>**

Often depression, delirium, and dementia can coexist. In such cases, delirium should be assessed and treated first, depression second, and dementia third.

<b>Parameter</b>	<b>Depression</b>	<b>Delirium</b>	<b>Dementia</b>
Onset	Weeks	Short/rapid, Abrupt, Hours/days	Months to years
Duration	3 to 6 months, may be chronic	Days to 3 weeks	5 to 15 years
Initial presentation	Flat affect, Hypochondriasis, Focuses on symptoms, Apathy, Little effort given to perform tasks	Disorientation, Clouded consciousness, Fluctuated moods, Disordered thoughts, Fails to understand tasks	Vague symptoms, Loss of intellect, Denies/conceals symptoms, Easily distracted, Great effort to perform tasks
Recent memory	Normal or recent/ past both altered	Patchy, Remote intact	Impaired, Concrete thinking
Intellect	Slowed, may be unwilling to respond	Impaired	Impaired, Bad/ inappropriate decisions, Denies problem
Judgment	Poor judgment, Many “don’t know” answers	Impaired, Difficulty separating facts & hallucinations	Impaired, Bad/ inappropriate decisions, Denies problem
Diurnal Pattern	Worse in morning, Sleep impaired	Day drowsiness, Nighttime hallucinations, Insomnia, Nightmares	Worse in evening, “Sundowning,” Reversed sleep
Attention Affect	Withdrawn, Constricted, Apathy, Hopeless, Distressed	Labile, Variable, Fear/panic, Euphoria, Disturbed	Easily distracted, Shallow, Labile, Inappropriate anxiety, Depression, Suspicious
Orientation	Intact	Disoriented, but usually not to person, Periods of lucidity	Disoriented
Level of consciousness	Intact	Disturbed	Intact
Psychotic symptoms	Delusions	Delusions	Late delusion, Hallucinations

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